UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/870,762	06/06/1997	BRADFORD J. DUFT	226/104US	7328

44638 7590 02/11/2008

Intellectual Property Department
Amylin Pharmaceuticals, Inc.
9360 Towne Centre Drive
San Diego, CA 92121

EXAMINER	
DEVI, SARVAMANGALA J N	
ART UNIT	**PAPER NUMBER**
1645	

MAIL DATE	DELIVERY MODE
02/11/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	08/870,762	DUFT ET AL.	
	Examiner	Art Unit	
	S. Devi, Ph.D.	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 October 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7 and 9-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7 and 9-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/23/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

RESPONSE TO APPLICANTS' AMENDMENT

Applicants' Amendment

1) Acknowledgment is made of Applicants' amendment filed 10/23/07 in response to the non-final Office Action mailed 04/23/07. With this, Applicants have amended the specification and the claims.

The Applicants' reference at pages 33 and 34 of their amendment filed 10/23/07 to and the traversal of the alleged rejection of claims 1, 5 and 7 under 35 U.S.C § 102(b) as being anticipated by Miltz (US 5,220,113); and Applicants' reference at pages 34 and 35 of their amendment filed 10/23/07 to and the traversal of the alleged rejection of claim 1 under 35 U.S.C § 102(b) as being anticipated by Waycott *et al.* (US 5,973,232) appear to be in error. No such patents teaching an iceberg lettuce cultivar were applied in the instant application.

Status of Claims

2) Claim 8 has been canceled via the amendment filed 10/23/07.

Claims 1, 6, 7, 10-14 and 16 have been amended via the amendment filed 10/23/07.

Claims 1-7 and 9-17 are pending and are under examination.

Information Disclosure Statement

3) Acknowledgment is made of Applicants' Information Disclosure Statement filed 10/23/07. Except for the reference of Chapman *et al.*, which has not been submitted, the information referred to therein has been considered, and a signed copy is attached to this Office Action.

Prior Citation of References

4) The references cited or used as prior art in support of one or more rejections in the instant Office Action and not included on an attached form PTO-892 or form PTO-1449 have been previously cited and made of record.

Objection(s) Withdrawn

5) The objection to the specification made in paragraphs 6(a) and 6(b) of the Office Action mailed 04/23/07 is withdrawn in light of Applicants' amendment to the specification.

Objection(s) Maintained

6) The objection to the specification made in paragraph 10(a) of the Office Action mailed 06/01/06 and maintained in paragraph 8 of the Office Action mailed 04/23/07 is still maintained for reasons set forth therein and herein below.

It is noted that Applicants have deleted Examples 20 and 21 from the specification which included a method of preparation of SEQ ID NO: 25 and SEQ ID NO: 24 respectively. Examples 9-19 continue to include the peptide synthetic 'methods of preparing' SEQ ID NO: 4-15 that have been recited in Table II. The specification as filed did not reference 'methods of preparing' SEQ ID NO: 4-15. As set forth previously, in order to incorporate material by reference, the host document/application must identify with detailed particularity what specific material it incorporates and clearly indicate where the material is found in the various documents. See *Advanced Display Systems, Inc. v. State Univ.*, 54 USPQ2d 1673 (Fed. Cir. 2000) citing *In re Seversky*, 177 USPQ 144, 146 (CCPA 1973). In the instant application, the only material that was particularly identified as being incorporated was the '[u]seful amylin agonist analogues' identified in the International Application, WPI Acc. No. 93-18488/22. See top of page 10 of the substitute specification. The methods of 'Preparation of' or synthesis of various amylin agonist analogues as recited in the newly added Examples of 9-19, were not materials specifically identified as being incorporated, in the instant specification. The objection stands.

Rejection(s) Maintained

7) The provisional rejection of claims 1-6 made in paragraph 10 of the Office Action mailed 11/13/00 under the judicially created doctrine of double patenting over the claims of the pending application, SN 09/445,517, and maintained in paragraph 9 of the Office Action mailed 05/30/02, paragraph 27 of the Office Action mailed 06/01/06, and paragraph 16 of the Office Action mailed 04/23/07, is still maintained for reasons set forth therein. Applicants state that a terminal disclaimer will be filed upon withdrawal of all other outstanding rejections.

8) The provisional rejection of claims 7, 13, 14 and 16 made in paragraph 37 of the Office Action mailed 06/01/06 and maintained in paragraph 17 of the Office Action mailed 04/23/07 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 33 of the co-pending application 09/445,517, is maintained for reasons set forth therein. Applicants' statement that they are willing to consider submitting a terminal disclaimer in the

present application with regard to the '517 application should this application issue as a patent prior to the present application has been noted.

9) The provisional rejection of claims 7, 14 and 16 made in paragraph 38 of the Office Action mailed 06/01/06 and maintained in paragraph 18 of the Office Action mailed 04/23/07 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 6 of the co-pending application, 10/851,574, is maintained for reasons set forth therein. Applicants' state that they are willing to consider submitting a terminal disclaimer in the present application with regard to the '574 application should this application issue as a patent prior to the present application.

Rejection(s) Withdrawn

10) The rejection of claim 14 made in paragraph 40 of the Office Action mailed 06/01/06 and maintained in paragraph 19 of the Office Action mailed 04/23/07 under 35 U.S.C § 112, first paragraph, as containing new subject matter, is withdrawn in light of Applicants' amendment to the claim.

11) The rejection of claims 9 and 10 made in paragraph 41 of the Office Action mailed 04/23/07 under 35 U.S.C § 112, first paragraph, as containing new matter, is withdrawn upon further consideration.

12) The rejection of claim 6 made in paragraph 44(a) of the Office Action mailed 04/23/07 under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

13) The rejection of claims 11-13 made in paragraph 44(b) of the Office Action mailed 04/23/07 under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

14) The rejection of claim 10 made in paragraph 44(c) of the Office Action mailed 04/23/07 under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

15) The rejection of claims 1, 7, 14 and 16 made in paragraph 44(d) of the Office Action mailed 04/23/07 under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in

light of Applicants' amendment to the claims.

16) The rejection of claims 2-6, 9-13, 15 and 17 made in paragraph 44(e) of the Office Action mailed 04/23/07 under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the base claim.

17) The rejection of claims 1-7, 9-14, 16 and 17 made in paragraph 45 of the Office Action mailed 04/23/07 under 35 U.S.C § 102(a) as being anticipated by Kolterman *et al.* (WO 96/40220, already of record) as evidenced by Tsanev (*Vutr. Boles* 23: 12-17, 1984, abstract, already of record), is withdrawn in light of Applicants' amendment to the claims and/or the base claims. Applicants' arguments have been considered, but are moot in light of the modified rejection set forth below under paragraph 33 and the reasoning provided therein.

18) The rejection of claims 7, 14, 16 and 17 made in paragraph 46 of the Office Action mailed 04/23/07 under 35 U.S.C § 102(e)(2) as being anticipated by Gaeta *et al.* (US 5,686,411, already of record) ('411) as evidenced by Tsanev (*Vutr. Boles* 23: 12-17, 1984, abstract, already of record), is withdrawn in light of Applicants' amendment to the claims and/or the base claims. Applicants' arguments have been considered, but are moot in light of the modified rejection set forth below under paragraph 35 and the reasoning provided therein.

19) The rejection of claims 1-7, 9, 11-14, 16 and 17 made in paragraph 47 of the Office Action mailed 04/23/07 under 35 U.S.C § 102(b) as being anticipated by Kolterman *et al.* (*Diabetologia* 39: 492-499, April, 1996, already of record) (Kolterman *et al.*, 1996) as evidenced by Itasaka *et al.* (*Psychiatr. Clin. Neurosci.* 54: 340-341, June 2000), is withdrawn in light of Applicants' amendments to the claims and/or the base claims. Applicants' arguments have been considered, but are moot in light of the modified rejection set forth below under paragraph 36 and the reasoning provided therein.

20) The rejection of claims 7, 14 and 16 made in paragraph 48 of the Office Action mailed 04/23/07 under 35 U.S.C § 102(e)(2) as being anticipated by Beumont *et al.* (US 5,321,008, already of record) ('008) as evidenced by Tsanev (*Vutr. Boles* 23: 12-17, 1984, abstract, already of record), is withdrawn in light of Applicants' amendments to the claims. Applicants' arguments have been considered, but are moot in light of the modified rejection set forth below under paragraph 34 and

the reasoning provided therein.

21) The rejection of claims 7, 14, 16 and 17 made in paragraph 38 of the Office Action mailed 04/23/07 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 34 and 35 of the US patent 5,686,411 issued to Gaeta *et al.* ('411, already of record) as evidenced by Tsanev (*Vutr. Boles* 23: 12-17, 1984, abstract), is withdrawn in light of Applicants' amendment to the claims and/or the base claims. Applicants' arguments have been considered, but are moot in light of the modified rejection set forth below under paragraph 26 and the reasoning provided therein.

22) The rejection of claims 7, 14 and 16 made in paragraph 39 of the Office Action mailed 04/23/07 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 11 and 13 of US patent 5,321,008 issued to Beumont *et al.* as evidenced by Tsanev (*Vutr. Boles* 23: 12-17, 1984, abstract, already of record) and Rink *et al.* (US 5,739,106, already of record) ('106), is withdrawn in light of Applicants' amendment to the claims and/or the base claims. Applicants' arguments have been considered, but are moot in light of the modified rejection set forth below under paragraph 27 and the reasoning provided therein.

23) The rejection of claim 14 made in paragraph 40 of the Office Action mailed 04/23/07 under 35 U.S.C § 112, first paragraph, as containing new matter, is withdrawn in light of Applicants' amendment to the claim. A modified rejection is set forth below to address the claim, as amended.

24) The rejection of claims 1, 7 and 16 made in paragraph 42 of the Office Action mailed 04/23/07 under 35 U.S.C § 112, first paragraph, as containing new matter, is withdrawn in light of Applicants' amendment to the claims. Applicants' arguments have been considered, but are moot in light of the rejection set forth below under paragraph 28 and the reasoning provided therein.

25) The rejection of claims 1-7 and 9-17 made in paragraph 43 of the Office Action mailed 04/23/07 under 35 U.S.C § 112, first paragraph, as being non-enabled with regard to the scope, withdrawn in light of Applicants' amendment to the claims. Applicants' arguments have been considered, but are moot in light of the rejection set forth below under paragraph 29 and the reasoning provided therein.

New Rejection(s) Necessitated by Applicants' Amendment

Double Patenting Rejection(s)

26) Claims 7, 14, 16 and 17 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 34 and 35 of the US patent 5,686,411 issued to Gaeta *et al.* ('411, already of record) as evidenced by Tsanev (*Vutr. Boles* 23: 12-17, 1984, abstract). Although the conflicting claims are not identical, they are not patentably distinct from each other.

The method of treatment claimed in claims 34 and 35 of the '411 patent includes administering to a mammal with diabetes mellitus a therapeutically effective amount of the amylin agonist of claim 19, ^{25,28,29}Pro-human amylin (SEQ ID NO: 1 or pramlintide). The portion of the disclosure of the '411 patent at lines 45-53 in column 7 supporting the limitation 'mammal' does not exclude, but expressly includes a patient seen by a medical practitioner, i.e., a human. The portion of the disclosure of the '411 patent at second paragraph under 'Summary of the Invention' supporting the limitations 'diabetes mellitus' and 'administration of .... an amylin agonist analogue' include insulin-requiring diabetes mellitus and administration of an amylin agonist analogue alone (i.e., consisting of) or in conjunction with (comprising or consisting essentially of) insulin or a glucagon, i.e., not in conjunction with another obesity relief agent. The portion of the disclosure of the '411 patent at lines 53-59 in column 8 supporting the limitation 'therapeutically effective amount' of the amylin agonist includes the dosage units of 0.1 to 5 mg or 0.5 to 1.0 mg of the amylin agonist. The amount effective to inhibit weight gain or induce weight loss, i.e., treat obesity, encompassed in the instant claims as described in the instant application of about 0.01 milligrams to about 5 milligrams per day, about 0.05 milligrams to about 2 milligrams per day, about 0.1 milligrams to about 1 milligram per day, or 300 micrograms per dose, falls within the range disclosed in the '411 patent. Given the art-known prevalence of intrinsic obesity in 80% to 90% of diabetic patients as disclosed by Tsanev, at least one of the human diabetic patients used in the method disclosed in the '411 patent qualifies as a human patient in need of treatment for obesity. Therefore, the method of the '411 patent comprising or consisting of the administration of 0.1 to 5 mg, or 0.5 to 1.0 mg of the amylin agonist, ^{25,28,29}Pro-human amylin alone or in conjunction with insulin or glucagon, to a diabetic human anticipates the instant claims. Given that the method step of the '411 patent and the instant claims are the same, the amylin agonist analogue pramlintide used

and its amount administered are the same, and the human diabetic patient used is the same, the method of the '411 patent is expected to bring about a weight gain-inhibiting effect, weight loss-inducing effect, or obesity-treating effect in the intrinsically obesity diabetic patient administered with a therapeutically effective amount of the pramlintide as claimed in the instant invention. Since the structural limitations of the instantly claimed method and all of the criteria required by the instant claims are met by the disclosure of Gaeta *et al.* ('411), Gaeta's ('411) method is expected to serve necessarily as the instantly claimed method and is expected to bring about the weight gain inhibiting effect, weight loss-inducing effect, or obesity-treating effect. **27)** Claims 7, 14 and 16 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 11 and 13 of US patent 5,321,008 issued to Beumont *et al.* as evidenced by Tsanev (*Vutr. Boles* 23: 12-17, 1984, abstract, already of record) and Rink *et al.* (US 5,739,106, already of record) ('106). Although the conflicting claims are not identical, they are not patentably distinct from each other.

The method of treatment claimed in claims 11 and 13 of the '008 patent includes administering to a human with type 2 diabetes mellitus a therapeutically effective amount of the amylin agonist calcitonin. The portion of the disclosure of the '008 patent at lines 14-17 in column 5; lines 8-11 and 49-54 in column 12; and lines 34 and 35 in column 2 that supports the claims includes subcutaneous administration to an insulin-requiring human who suffers from Type 1 or Type 2 diabetes mellitus a therapeutically effective amount of an amylin agonist *alone* such as calcitonin (i.e., consisting of), or calcitonin and insulin (i.e., comprising or consisting essentially of), contained in a pharmaceutically acceptable carrier. The portion of the disclosure of the '008 patent at first full paragraph in column 13 of the '008 patent supporting the 'therapeutically effective amount' includes the typical dosage units of about 0.1 to 1 mg of calcitonin. The amount effective to treat obesity, the amount effective to inhibit weight gain, or the amount effective to induce weight loss encompassed in the instant claims as described in the instant application, for example, about 0.01 milligrams to about 5 milligrams per day, about 0.05 milligrams to about 2 milligrams per day, or 300 micrograms per dose, falls within the range of the therapeutically effective amount disclosed in the '008 patent. Given the art-known prevalence of intrinsic obesity in 80% to 90% of diabetic patients as disclosed by Tsanev (see abstract), at

least one insulin-requiring human diabetic patient used in the method disclosed in the above-identified claims claimed in the '008 patent qualifies as a human patient in need of treatment for obesity. Therefore, the method of the '008 patent comprising the administration of about 0.1 to 1 mg of calcitonin to an insulin-requiring diabetic human anticipates the instant claims. Given that the method step of the '008 patent and the instant claims is the same, and the amylin agonist calcitonin administered and the amount administered are the same, and the human diabetic patient to whom calcitonin is administered is the same as the one described in the instant application, the method claimed in the '008 patent is expected to bring about an obesity-treating effect, weight gain-inhibiting effect, or weight loss-inducing effect in the intrinsically obese calcitonin-treated diabetic patient of the '008 patent. Since the structural limitations of the instantly claimed method and all of the criteria required by the instant claims are met by the teachings of the '008 patent, Beumont's ('008) method is expected to serve necessarily as the instantly claimed method and is expected to bring about the obesity-treating effect, weight gain inhibiting effect, or weight loss-inducing effect. The art-recognized intrinsic obesity being prevalent in 80 to 90% of diabetic patients as disclosed by Tsanev (see abstract), Beumont's ('008) method of administration of the above-identified therapeutically effective amount (i.e., dosage units of about 0.1 to 1 mg) of the amylin agonist of calcitonin to at least one intrinsically obese type 2 diabetic human subject anticipates the instant claims.

Rejection(s) under 35 U.S.C. § 112, First Paragraph (New Matter)

28) Claims 1, 7, 14 and 16 and the dependent claims 2-6, 9-13, 15 and 17 are rejected under 35 U.S.C § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claims 1, 7 and 16, as amended, include the new limitations: an amount 'effective to inhibit weight gain or induce weight loss ..... said subject is in need of treatment of obesity'. Claim 14, as amended, includes the new limitation: an amount effective to treat obesity 'in said subject by inhibiting weight gain or inducing weight loss wherein said subject is in need of treatment for obesity'. As claimed currently, 'an amount effective to inhibit weight gain or induce weight loss in

said human subject' is not the amount of the recited amylin or the amylin agonist, but of the composition that 'comprises' an amylin, amylin agonist, or an amylin agonist analogue plus a pharmaceutically acceptable carrier plus any other element that is comprised within the composition. Applicants state that the amendment to claims 1, 7, 14 and 16 find support at page 9, lines 9-11 and 15-16, and page 22, lines 27-28 of the specification. However, lines 9-11 and 15-16 of page 9 of the specification are not supportive of 'an amount effective to inhibit weight gain ..... in said human subject .....' or 'an amount of a composition comprising a pharmaceutically acceptable carrier and an amylin or an amylin agonist effective to inhibit weight gain or induce weight loss in said human subject'. The description at lines 27 and 28 of page 22 of the specification is limited to therapeutically effective amounts of amylin or amylin agonist analogue for use in the control of obesity, which are described as those that decrease body weight. An 'amount effective to inhibit weight gain' is an amount effective in maintaining the body weight as it existed prior to the treatment, for which there is no support. The specification does not support the new limitation of an amount of an amylin or an amylin agonist 'effective to inhibit weight gain' in a human subject in need of treatment for obesity or 'an amount of a composition comprising a pharmaceutically acceptable carrier and an amylin or an amylin agonist effective to inhibit weight gain or induce weight loss in said human subject'. Furthermore, there is lack of descriptive support for an amount of a salt of amylin or an amylin agonist compound and its administration to a human subject in need of treatment for obesity wherein the amount of the salt compound is effective to treat obesity in said subject by inhibiting weight gain or inducing weight loss, wherein the salt compound is not administered in conjunction with another obesity relief agent, as claimed currently in the amended claim 14. Furthermore, the amended claim 1 continues to include the limitation: 'method of treating obesity .... consisting of administering .... an amount effective to inhibit weight gain or induce weight loss ..... of composition comprising an amylin or an amylin agonist and a pharmaceutically acceptable carrier'. A method of treatment of obesity 'consisting of' such an administration step *excludes,* for example, simultaneous insulin administration, or insulin administration minutes or hours before or after the administration. However, neither the original six claims, nor the description of the novel methods of treatment of the instant invention support such a method of treating obesity 'consisting of' administering an effective ..... composition comprising an amylin or an amylin agonist and a

pharmaceutically acceptable carrier. For example, the originally filed specification at lines 6-8 of page 9 of the specification states [Emphasis added]:

> The present invention is directed to novel methods for treating or preventing obesity in humans *comprising* the administration of an amylin or an amylin agonist, the amylin agonist analogue ^{25,28,29}Pro-human amylin.

Pages 30-31 and Table I describe a statistically significant reduction in the mean baseline weight seen after the subcutaneous administration of 60 micrograms TID or 60 micrograms QID of one specific amylin agonist analogue species, pramlintide, to type II diabetic subjects for four weeks, wherein said pramlintide administration was accompanied *with the continued administration of insulin*. The method of treatment of obesity as described in the originally filed specification comprised insulin treatment *and* the administration of a specific dose of pramlintide to type II diabetic patients. This however does not provide descriptive support for the now claimed method of treating obesity in a human in need of treatment for obesity, said method 'consisting' of administering to said subject an amount of a composition as recited comprising an amylin or any amylin agonist and a pharmaceutically acceptable carrier, wherein said amount of the composition is effective to inhibit weight gain or induce weight loss in said subject. Therefore, the above-identified limitations in the claims are considered to be new matter. *In re Rasmussen*, 650 F2d 1212 (CCPA, 1981). New matter includes not only the addition of wholly unsupported subject matter but also, adding specific percentages or compounds after a broader original disclosure, or even omission of a step from a method. See M.P.E.P. 608.04 to 608.04(c).

Applicants are invited to point to the descriptive support in specific pages and lines of the disclosure, as originally filed, for the limitation identified above, or alternatively, remove the new matter from the claim(s). Applicants should specifically point out the support for any amendments made to the disclosure. See MPEP 714.02 and 2163.06.

Rejection(s) under 35 U.S.C § 112, First Paragraph (Scope of Enablement)

29) Claims 1-7 and 9-17 are rejected under 35 U.S.C § 112, first paragraph, because the specification, while being enabling for a method of reducing the body weight of an insulin-taking type 2 diabetic human subject having a body weight not varying more than 45% from the desirable weight, by subcutaneous administration to said subject, within 15 minutes of each meal, an amount

of the amylin agonist analogue species, ^{25,28,29}Pro-h-amylin (SEQ ID NO: 1), i.e., pramlintide, wherein said pramlintide is not in conjunction with another obesity relief agent, and wherein said amount of the pramlintide significantly reduces the mean body weight of said human subjects after four weeks of said treatment compared to the mean body weight of said subject prior to said treatment, does not reasonably provide enablement for a method of treating obesity in any human subject including a non-diabetic human subject in need of treatment for obesity, or a diabetic human subject in need of treatment for obesity who is not on insulin therapy, comprising or consisting of administering a generic amylin, a generic amylin agonist other than calcitonin or CGRP, or any 'amylin agonist analogue' other than pramlintide, as claimed in a broad sense. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with the claims.

Instant claims are evaluated based on *Wands* factors. Many of the factors regarding undue experimentation have been summarized in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Circ. 1988) as follows:

- The quantity of experimentation necessary (time and expense);
- The amount of direction or guidance presented;
- The presence or absence of working examples of the invention;
- The nature of the invention;
- The state of the art;
- The relative skill of those in the art;
- The predictability or unpredictability in the art; and
- The breadth of the claims.

In the instant application, the nature of the invention is pertinent to the treatment of obesity in a human subject in need of such treatment comprising or consisting of administering an amylin, an amylin agonist, or an amylin agonist analogue composition or compound in an amount effective to inhibit weight gain or induce weight loss in said subject. As described in the instant specification, the state of the art recognizes obesity or adiposity to be a 'chronic disease' that is highly prevalent in modern society which is strongly associated with multiple conditions including diabetes mellitus, insulin resistance, hypertension etc. The breadth of the claimed method encompasses the following. The limitation 'obesity' encompasses diabetes-associated obesity, non-diabetes-associated obesity, obesity associated with family genetics, morbid obesity, aging-associated obesity, insulin requiring obesity, obesity due to hypernutrition etc. The step recited in

claim 1 'consists of' administering to said human subject an amount effective to inhibit weight gain (i.e., maintain the existing weight) or an amount effective to induce weight loss in said human subject of a composition 'comprising' a pharmaceutically acceptable carrier and an amylin or an amylin agonist. Such an administration step *excludes* simultaneous insulin administration, or insulin administration before or after the administration of an amylin, amylin agonist, or an amylin agonist analogue. Because of the open claim language 'comprising', the composition recited in claims 1 and 2 is allowed to comprise one or more obesity relief agents or any other compounds. As claimed currently, 'an amount effective to inhibit weight gain or induce weight loss in said human subject' is not the amount of the recited amylin or the amylin agonist, but of the composition that 'comprises' an amylin, amylin agonist, or an amylin agonist analogue plus a pharmaceutically acceptable carrier plus any other element that is comprised within the composition. 'Therapeutically effective amounts' of an amylin, an amylin agonist, or an amylin agonist analogue, for use in the control of obesity are described in the specification as 'those that decrease body weight', but are not described as amounts that inhibit weight gain, i.e., an amount that maintains the weight as existed prior to the treatment. See last full sentence on page 22 of the instant specification. The method of treating obesity in a human subject in need of treatment for obesity as claimed in the independent claim 7 'comprises' administering to said subject an amount of a composition comprising a pharmaceutically acceptable carrier and an obesity relief agent 'consisting' of an amylin or an amylin agonist in an amount effective to inhibit weight gain or induce weight loss in said human subject and is effective to treat obesity. The method of treating obesity in a human subject in need of treatment for obesity as claimed in the independent claim 14 'comprises' administering to said subject a compound selected from the group consisting of an amylin, an amylin agonist, and salts thereof, wherein the compound including the salt compound is administered in an amount effective to treat obesity by inhibiting weight gain or inducing weight loss and wherein said compound is not administered in conjunction with another obesity relief agent. The method of treating obesity in a human subject in need thereof as claimed in the independent claim 16 'comprises' administering to said subject an effective amount of a 'composition consisting essentially of an amylin or an amylin agonist, wherein said amount' of the composition is effective to treat obesity by inhibiting weight gain or inducing weight loss in said

subject. The instant disclosure lacks a specific definition for the limitation 'a composition consisting essentially of an amylin or an amylin agonist' as to what it excludes or includes, and therefore one cannot envisage whether or not the composition includes or excludes an element such as insulin, glucagon, an anti-diabetic agent, or a gastric emptying agent etc. The limitation 'a human subject ... in need of treatment for obesity' encompasses an overweight, moderately obese, morbidly obese, diabetic and non-diabetic obese, insulin-requiring and insulin non-requiring obese human subject as well as a human subject with natural aging-associated obesity. The limitations 'amylin agonist' and 'amylin agonist analogue' broadly encompass a myriad of compounds, including a peptide and a nonpeptide compound (see paragraph bridging pages 13 and 14 of the original specification), non-human amylins, amylins having amino acid modifications or substitutions, variants of amylin, and the art-accepted amylin agonists such as calcitonin and CGRP (see lines 45-47 in column 7 of US patent 5,739,106 and claims 3 and 10 of US 5,175,145, both already of record) etc. At least a representative number of the species encompassed within the scope of the instantly claimed method is *required* to be effective in treating obesity in a diabetic or non-diabetic human subject, or a morbidly or non-morbidly obese human subject when administered not in conjunction with another obesity relief agent in the recited amount or dose range.

With regard to enablement, a review of the instant specification indicates that Examples 2-4 and 9-20 are not enabling of the claimed method of treatment. These Examples describe how to prepare selective amylin agonist analogues. Example 5 pertains to the evaluation of *in vitro* binding of compounds to amylin receptors whereas Example 6 pertains to the determination of amylin agonist activity of the compounds as measured by soleus muscle assay. Examples 7 and 8 describe methods of measuring gastric emptying using phenol red and tritiated glucose gastric emptying assays. However, what are claimed are not amylin agonist analogues or a method of making them, or using them in *in vitro* assays as described in Examples 2-4 and 9-20 of the instant specification, but a method of treating obesity in a mammal in need of treatment for obesity by administering *in vivo* a weight gain-inhibiting effective amount or a weight loss-inducing effective amount of an amylin, amylin agonist, or amylin agonist analogue. Example 1 of the instant specification indicates that the human subjects used the instant invention are those with a history of type 2 diabetes mellitus,

who *required* insulin treatment for at least 6 months prior to the pre-screening visit. Body weight-wise, i.e., obesity-wise, these patients are described as having a body weight not varying more than 45% from the 'desirable weight' before admission into the study based upon Metropolitan Life Tables. The only amylin agonist analogue species that was administered to these type 2 diabetic patients was ^{25,28,29}Pro-h-amylin (SEQ ID NO: 1), also known as pramlintide. Groups of patients were given separate mealtime pramlintide, 30 micrograms QID; 60 micrograms QID, or 60 micrograms TID subcutaneously before 15 minutes of each meal three to four times a day. Patients *remained on their insulin, usual diet, and exercise regimens* and therefore the method comprised administration of pramlintide as explained above, along with the administration of insulin. The study period was limited to four weeks, i.e., 28 days, and the outcome was determined by comparing, at the end of four weeks, the mean body weight of the treated diabetic subjects with the mean body weight of the subject prior to the treatment. Thus, the originally filed specification at pages 30-31 and Table I describes a statistically significant reduction in the mean baseline weight seen after the subcutaneous administration of 60 micrograms TID or 60 micrograms QID of one specific amylin agonist analogue species, pramlintide, to type 2 diabetic subjects for four weeks, wherein said pramlintide administration was accompanied with the continued use of insulin. The method as described in the originally filed specification thus comprised insulin treatment *and* the administration of a specific dose of pramlintide in type 2 diabetic patients via a specific route. The decrease in body weight observed was statistically significant compared to the body weight of those type 2 diabetes patients who were treated with insulin alone. However, this single enabled embodiment is not representative of the full scope of the claims which broadly encompasses the administration of any amylin, any amylin agonist, or any of a plethora of non-pramlintide amylin agonist analogues in the treatment of obesity in diabetic and non-diabetic patients not on insulin treatment. While there is no requirement for Applicants to enable all of the amylin agonist or amylin agonist analogue species encompassed within the claimed invention, enablement of a reasonable number such species in the claimed method is required. This is critically important at the time of the invention, because there is no predictability that if one used an amylin, amylin agonist, or a non-pramlintide amylin agonist analogue in place of Applicants' pramlintide in type 2 diabetic or non-diabetic overweight or obese subjects who are on or not on insulin treatment, or morbidly obese human subjects who are on or not

on insulin therapy, the administered amylin, amylin agonist, or non-pramlintide amylin agonist analogue would bring about significant or clinically meaningful weight loss-inducing, weight gain-inhibiting, or obesity-relieving effect. Neither the state of the art *at the time of the invention*, nor the instant specification as originally filed, provides specific guidance and direction with regard to the use of a generic amylin, or a non-pramlintide or non-calcitonin amylin agonist, or a non-pramlintide amylin agonist analogue to treat obesity in any human subject in need of treatment for obesity.

Upon consideration of the evidence as a whole and analysis of all of the *Wands* factors, the instantly claimed method is viewed as being non-enabled with regard to the full scope. It should be noted that the scope of the required enablement varies inversely with the degree of predictability involved. A single embodiment may provide broad enablement in cases involving predictable factors. However, in applications directed to inventions in arts where results are unpredictable, the disclosure of a single species does not provide an adequate basis to support generic claims. MPEP § 2164.03. However, in cases involving unpredictable factors, such as most chemical reactions and physiological activity, more may be required. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) (contrasting mechanical and electrical elements with chemical reactions and physiological activity). See also *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); *In re Vaeck*, 947 F.2d 488, 496, 20 USPQ2d 1438, 1445 (Fed. Cir. 1991). This is because it is not obvious from the disclosure of one species, what other species will work. In the instant case, it is not obvious from the disclosure of the administration of pramlintide species in the treatment of obesity in type 2 diabetic humans, what other non-pramlintide species or salts thereof would work in treating obesity in diabetic or non-diabetic humans in need of treatment of obesity. It should be noted that predictability or unpredictability is one of the *Wands* factors to be considered for enablement or lack thereof under 35 U.S.C § 112, first paragraph. The instantly claimed invention is in an area of art that is unpredictable. Amylin, a sufficient number of non-pramlintide amylin agonist analogues, and salts thereof, are not enabled as obesity relief agents in the instantly claimed method. With regard to the therapeutic use of amylin, the state of the art indicates the difficulty, the undesirable pharmacological properties, and the impracticability of using amylin, including human amylin, clinically as 'a therapeutic agent'. For instance, Baron *et al.* (*Current Drug Targets – Immune, Endocrine & Metabolic Disorders* 2(1): 63-82, 2002, already of record) taught

the following with regard to the clinical use of amylin as a therapeutic agent:

> Clinical use of amylin as a therapeutic agent is considered impractical because of its instability in solution and its propensity to aggregate and adhere to surfaces, properties that hamper the manufacturing, formulation, and storage of this peptide as a drug. Pramlintide is a synthetic, equipotent analogue of human amylin in which the undesirable pharmacological properties of human amylin (insolubility, tendency to self-aggregate) have been overcome by replacement of the three amino acid residues .... with prolines ....

Ratner *et al.* (*Diabetes Technol. Ther.* 4: 51-61, 2002, already of record) provide a similar teaching (see paragraph bridging the two columns on page 52):

> Native human amylin is not ideal for clinical use because of the peptide's poor solubility and propensity to aggregate.

Applicants state that Baron *et al.* and Ratner *et al.* support enablement of the claimed invention (see page 31 of Applicants' amendment filed 10/23/07), but fail to explain how these references enable a method of administering amylin or any non-pramlintide amylin agonist analogue to a human for treating obesity.

A specification disclosure which contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as being in compliance with the enablement requirement of 35 U.S.C. 112, first paragraph, *unless* there is a reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support. Assuming that sufficient reason for such doubt exists, a rejection for failure to teach how to make and/or use will be proper on that basis. *In re Marzocchi*, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA 1971).
In the instant case, one of the reasons for doubting the objective truth of the statements comes from Applicants' own statement. For example, with regard to the state of the art at the time of the invention, Applicants have previously gone on the record with the following (see pages 9, 13 and 14 of Applicants' Appeal Brief filed July 2000) [Emphasis in original]:

> .... THE RINK PATENT PROVIDES THAT AMYLIN AND AMYLIN AGONISTS ADMINISTERED AS DESCRIBED AND CLAIMED IN THE PRESENT APPLICATION HAVE "NO MEASURABLE EFFECT" ON FOOD INTAKE.
>
> .... the Rink patent reports that a 1.0 μg/kg dose (equivalent to about 70μg/dose in an adult human) had no effect on food intake.

The Rink patent that is being referred to by Applicants in the Appeal Brief is US 5,739,106 (already of record). Note that the above-mentioned about 70 μg/dose in an adult human is encompassed

within the therapeutic amount range of about 0.01 to about 5 mg, or about 0.05 to about 2 mg of amylin, as recited in instant claims 12 and 13. Applicants have not advanced any arguments with regard to this issue raised in the previous Office Action. Thus, in view of the above-cited acknowledgment of the failure of amylin to have any effect on food intake, one of skill in the art would look into Applicants' specification for guidance and direction. However, the instant specification fails to show that human or non-human amylin or a salt thereof, or a composition comprising, consisting of, or consisting essentially of the same, was in fact stable, soluble and/or non-aggregating enough to be 'therapeutic' in a method of treating obesity upon administration in any amount and by any route, with or without concurrent insulin therapy, to a diabetic or non-diabetic human subject in need of treatment for obesity. With regard to the quantity of experimentation needed, the standard for determining whether the specification meets the enablement requirement was cast in the Supreme Court decision of *Mineral Separation v. Hyde*, 242 U.S. 261, 270 (1916) which postured the question: 'is the experimentation needed to practice the invention undue or unreasonable'. That standard is still the one to be applied. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). In the instant case, no guidance or direction has been provided in the instant specification so that one could predict which of the amylin agonist analogue species other than pramlintide would have the requisite therapeutic effect against obesity. Because there is no way to predict *a priori* which amylin agonist analogues from the specification or the chemical structures alone would be therapeutically active against obesity in diabetic or non-diabetic humans subjects, including morbidly obese human subjects, an extraordinary amount of trial and error experimentation is required to identify the obesity-treating amylin agonist analogue species. Assuming *arguendo* that the experimentation required is routine, and if one of skill in the art screens innumerable non-pramlintide amylin agonist analogue species currently encompassed within the recited genus, including those disclosed in Examples 2 and 3 or Table II of the instant invention, using receptor binding assays and assays for amylin activity, there is absolutely no predictability that a non-pramlintide amylin agonist analogue having amylin activity would have a weight loss-inducing effect, obesity-relieving effect, or food intake-reducing effect given the Applicants' admission that amylin itself has no effect on food intake. Given this and the lack of showing within the instant specification, the weight loss-inducing or weight gain-inhibiting effect of any amylin or any non-

pramlintide amylin agonist analogue mimicking an effect of amylin, administered alone or as an adjunct to insulin therapy, to an obese diabetic or obese non-diabetic human subject, is simply not predictable. Applicants have provided no guidance with regard to the use of extraordinarily large genus of amylins, amylin agonists, and amylin agonist analogues in the treatment of obesity in humans. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) states: 'The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art'. The amount of guidance or direction refers to that information in the application, as originally filed, that teaches exactly how to make or *use* the invention. The more is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling' (MPEP 2164.03). MPEP also states that physiological activity can be considered inherently unpredictable. Whether the specification would have been enabling *as of the filing date* involves consideration of the nature of the invention, the state of the prior art, and the level of skill in the art. The initial inquiry is into the nature of the invention, i.e., the subject matter to which the claimed invention pertains. The nature of the invention becomes the backdrop to determine the state of the art and the level of skill possessed by one skilled in the art. The state of the prior art is what one skilled in the art would have known, *at the time the application was filed*, about the subject matter to which the claimed invention pertains. The relative skill of those in the art refers to the skill of those in the art in relation to the subject matter to which the claimed invention pertains *at the time the application was filed*. See MPEP § 2164.05(b). The post-filing abstracts of Aronne *et al.* (*Obesity* 14: A17, 2006 – Applicants' IDS) and Smith *et al.* (*Diabetes* 56: A88, 2007 – Applicants' IDS) submitted by Applicants are silent about the diabetic or non-diabetic status of the subjects included in the study. Both are limited to the use of the single amylin agonist analogue species, pramlintide in the method described therein. The post-filing teachings of Aronne *et al.* (*J. Endocrinol. Metabol.* 92: 2977-2983, 2007 – Applicants' IDS) and Smith *et al.* (*J. Am. J. Physiol. Endocrinol. Metabol.* 293: 620-627, 2007 – Applicants' IDS) submitted by Applicants are also limited to the use of one amylin agonist analogue species,

pramlintide, for reducing caloric intake and meal size, or for reducing body weight. These two post-filing publications support the Office's position on lack of enablement of the full scope of the instant claims by confirming that even about a decade after the effective filing date of the instant application, the only amylin agonist analogue species within the recited broad genus that is being used for inducing weight loss in humans is pramlintide. None of these post-filing references and abstracts represents the state of the art *at the time of filing*. Contrary to Applicants' allegation, a *prima facie* case of lack of scope of enablement has been established by providing sufficient references and specific technical reasons along with the documentation of Applicants' own previous statement indicating that an amylin, amylin agonist, or amylin agonist analogue mimicking an effect of amylin does not necessarily have an effect on food or caloric intake, and therefore does not necessarily have an anti-obesity effect. Thus, in view of level of skill, the state of the art at the time of the invention, and the information in the specification, one of skill would *not* expect that the recited genus could be used in that manner without undue experimentation. For the reasons delineated above and due to the lack of specific direction or guidance within the instant specification, the breadth of the claims, the absence of working examples enabling the full scope, the art-recognized unpredictability factor, and the quantity of the experimentation necessary, a considerable amount of non-routine undue experimentation would have been required to reproducibly practice the full scope of the invention, as claimed. Instant claims do not meet the scope of enablement provisions of 35 U.S.C. § 112, first paragraph. The scope of enablement provided to one skilled in the art is not commensurate with the scope of protection sought by the instant claims.

Rejection(s) under 35 U.S.C. § 112, Second Paragraph

30) The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude one or more claims particularly pointing out and distinctly claiming the subject matter which the Applicant regards as his/her invention.

31) Claims 16 and 17 are rejected under 35 U.S.C § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

(a) Claim 16 is indefinite, confusing, and/or redundant in the limitations: 'amount effective to inhibit weight gain or induce weight loss in said subject' (see lines 2 and 3) and

'effective to treat obesity by inhibiting weight gain or inducing weight loss in said subject' (see lines 4 and 5).

(b) Claim 17, which depends from claim 16, is also rejected as being indefinite because of the indefiniteness identified above in the base claim.

Rejection(s) under 35 U.S.C. § 102

32) The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> **(a)** the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
> **(b)** the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> **(e)** the invention was described in-
> **(2)** a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

33) Claims 1-7, 9-14, 16 and 17 are rejected under 35 U.S.C § 102(a) as being anticipated by Kolterman *et al.* (WO 96/40220, already of record) as evidenced by Tsanev (*Vutr. Boles* 23: 12-17, 1984, abstract, already of record).

Kolterman *et al.* ('220) taught a method of administering to an insulin-taking type II diabetic human subject a dose of 10, 30, 50, 60 or 150 micrograms per day (i.e., the amount falling in the range recited in the instant claims) of the amylin agonist composition, pramlintide or $^{25, 28, 29}$pro-h-amylin, also known as AC137 (i.e., SEQ ID NO: 1), i.e., the same amylin agonist administered in the instantly claimed method. The composition consists of pramlintide and a pharmaceutically acceptable carrier, and is administered in single or multiple doses, for example, of about 30 micrograms QID, or about 60 micrograms TID or QID, i.e., an amount effective to inhibit weight gain or induce weight loss. See pages 9-11; paragraph bridging pages 20 and 21; page 21; first paragraph on page 19; lines 8-10 on page 19; and the first row reciting 'Insulin-Treated Patients' in each Table of Kolterman *et al.* ('220). Pramlintide is administered subcutaneously 1-4 times a day, before meals. See pages 9 and 22. Kolterman *et al.* ('220) additionally taught that the presence of obesity is a characteristic of 'most patients with Type II diabetes mellitus'. See page 10. Kolterman *et al.* ('220) taught the benefit of obtaining weight loss in Type II diabetic patients by teaching that

hyperglycemia associated with Type II diabetes can be reversed or ameliorated by weight loss sufficient to restore the sensitivity of the peripheral tissues to insulin (see pages 7, first paragraph), thus teaching that Type II diabetic patients are in need of weight loss or treatment of obesity. Thus, the very active step of the instantly claimed method was disclosed and practiced by Kolterman *et al.* ('220) in 1996 in the very same patient, i.e., a human type II diabetes mellitus patient used by Applicants in Example 1 of the instant application. The prior art method is the *same* as the instantly claimed method in terms of the amylin agonist or the amylin agonist analogue, the amylin agonist composition, or the amylin agonist analogue composition (pramlintide) administered, and the insulin-taking Type II diabetic patient used (80-90% of Type II diabetic patients being known in the art to be intrinsically obese as taught by Tsanev - see Tsanev's abstract), the subcutaneous route of administration used, the dose and the daily frequency of the amylin agonist pramlintide administered, and the administration step prior to meals. Given Tsanev's express disclosure that 80 to 90% of type II diabetic patients are intrinsically obese, and given Kolterman's ('220) recognition that obesity is an intrinsic characteristic of most patients with Type II diabetes mellitus and the indication that these patients are in need of weight loss, Kolterman's ('220) method of subcutaneous administration of pramlintide to at least one Type II diabetic patient in an amount that falls within the range recited in the instant claims, necessarily serves as the claimed method of treating obesity and therefore anticipates the instantly claimed method. Since 80-90% of Type II diabetic patients are known in the art to be obese, at least one of Kolterman's ('220) type II diabetic patients to whom pramlintide composition is administered, necessarily qualifies as a human subject in need of treatment of obesity as recited in the instant claims. Since the structural limitations of the instantly claimed method and all of the criteria required by the instant claims are met by the teachings of Kolterman *et al.* ('220), Kolterman's ('220) method is expected to serve necessarily as the instantly claimed method and is expected to bring about the obesity-treating effect, weight gain inhibiting effect, or weight loss-inducing effect. The Office's position that Kolterman's ('220) method is the same as the Applicants' claimed method is based upon the fact that the method step, the pramlintide compound administered, the amount of the compound administered, the route by which the compound is administered, and the at least one intrinsically obese diabetic human patient to which the pramlintide compound is administered, are the *same* in the two methods. The art-recognized intrinsic obesity being prevalent

in 80 to 90% of diabetic patients as disclosed by Tsanev (see abstract), Kolterman's ('220) method of administration of the above-identified therapeutically effective amount (i.e., about 30 micrograms QID, or about 60 micrograms TID or QID, or a dose of 10, 30, 50, 60 or 150 micrograms per day) of the amylin agonist ^{25,28,29}Pro-human amylin to at least one intrinsically obese type 2 diabetic human subject anticipates the instant claims. Given that the method step of the Kolterman's ('220) method and the instant claims are the same, Kolterman's ('220) method is expected to bring about weight gain-inhibiting or weight loss-causing therapeutic effect in the intrinsically obese pramlintide-treated type II diabetic patient. Since the Office does not have the facilities for examining and comparing Applicants' claimed method with that of the prior art, the burden is on Applicants to show a novel difference between the claimed method and the method of the prior art. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald et al.*, 205 USPQ 594. MPEP 2112 refers to *In re Best* to explain that something which is old does not become patentable upon the discovery of a new property; 'the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. *In re Best*, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977)'. Since the prior art clearly teaches the instantly claimed method, any assertions of specific functional properties attributed to the amylin agonist pramlintide in the claimed method are merely inherent and do not necessarily make the claimed method patentable.

Claims 1-7, 9-14, 16 and 17 are anticipated by Kolterman *et al.* ('220). The publication of Tsanev is **not** used as a secondary reference in combination with the reference of Kolterman *et al.* ('220), but rather is used to show that every element of the claimed subject matter is disclosed by Kolterman *et al.* ('220), with the unrecited limitation(s) being inherent as evidenced by the state of the art. See *In re Samour* 197 USPQ 1 (CCPA 1978). 'To serve as an anticipation when the reference is silent about the asserted inherent characteristic, such gap in the reference may be filled with recourse to extrinsic evidence. Such evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill.' *Continental Can Co. USA v. Monsanto Co.*, 948 F.2d 1264, 1268, 20 USPQ2d 1746, 1749 (Fed. Cir. 1991). Note that as long as there is evidence of record establishing inherency, failure of those skilled in the art to contemporaneously recognize an

inherent property, function or ingredient of a prior art reference does not preclude a finding of anticipation. *Atlas Powder Co. v. IRECO Inc.*, 190 F.3d 1342, 1349, 51 USPQ2d 1943, 1948 (Fed. Cir. 1999). See MPEP 2124. Tsanev's extrinsic evidence makes clear that the missing descriptive matter, i.e., prevalence of obesity in at least one of Kolterman's ('220) diabetic subjects administered with pramlintide, is necessarily present in the thing described by Kolterman *et al.* ('220). The method of Kolterman *et al.* ('220) clearly anticipates the claimed method of the instant invention, because Kolterman *et al.* ('220) taught the very step of the instantly claimed method in the very same human patient population. The alleged failure of Kolterman ('220) to expressly mention treatment of obesity as a goal is irrelevant. To the extent the method embodiment in the claimed invention achieves treatment of obesity, so does the method of Kolterman's ('220). Where the result is a necessary consequence of what was deliberately intended, it is of no import that the article's authors did not appreciate the results. See *Mehl/Biophile International Corp. v. Milgraum*, U.S. Court of Appeals Federal Court, 52 USPQ2d 1303 and 1306, 192 F3d 1362, 1999 citing *W.L. Gore & Assocs. v. Garlack, Inc.*, 721 F.2d 1540, 1548, 220 USPQ 303, 309 (Fed. Cir. 1983).

34) Claims 7, 14 and 16 are rejected under 35 U.S.C § 102(e)(2) as being anticipated by Beumont *et al.* (US 5,321,008, already of record) ('008) as evidenced by Tsanev (*Vutr. Boles* 23: 12-17, 1984, abstract, already of record).

The limitation in claim 16: 'a composition consisting essentially of an amylin or an amylin agonist' and the limitation in claim 14: 'method ... comprising ..... wherein said compound is not administered in conjunction with another obesity relief agent' do not exclude the administration of an anti-diabetic agent, insulin, glucagon, a gastric emptying-inhibiting agent such as exendin etc. It is further noted that 'amylin agonist' is defined in the instant specification as a peptide or non-peptide compound that mimics the effect of amylin. See paragraph bridging pages 13 and 14 of the originally filed specification. Calcitonin and CGRP are described in the instant specification as sharing the food intake-suppressing action or effect of peripherally or centrally administered amylin. See paragraph bridging pages 9 and 10 of the originally filed specification.

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e).

This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 C.F.R 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention 'by another', or by an appropriate showing under 37 C.F.R 1.131.

Beumont *et al.* ('008) taught a method of subcutaneous administration to an insulin-requiring human who suffers from Type 1 or Type 2 diabetes mellitus a therapeutically effective amount of an amylin agonist *alone* such as calcitonin, or calcitonin and insulin, contained in a pharmaceutically acceptable carrier. See claims 11, 7, 13 and 4; lines 14-17 in column 5; lines 8-11 and 49-54 in column 12; and lines 34 and 35 in column 2. Claim 11 of the '008 patent is directed to the method of administering a therapeutically effective amount of the amylin agonist calcitonin to an insulin-requiring human with diabetes mellitus. The 'therapeutically effective amount' taught by Beumont *et al.* ('008) includes the typical dosage units of about 0.1 to 1 mg of calcitonin. See first full paragraph in column 13. The amount effective to treat obesity, the amount effective to inhibit weight gain, or the amount effective to induce weight loss encompassed in the instant claims as described in the instant application of about 0.01 milligrams to about 5 milligrams per day, about 0.05 milligrams to about 2 milligrams per day, or 300 micrograms per dose, falls within the range of the therapeutically effective amount disclosed in the '008 patent. Given the art-known prevalence of intrinsic obesity in 80% to 90% of diabetic patients as disclosed by Tsanev (see abstract), at least one diabetic patient used in the method disclosed in the '008 patent qualifies as a human patient in need of treatment for obesity. Therefore, the method of the '008 patent comprising the administration of about 0.1 to 1 mg of calcitonin to a diabetic human anticipates the instant claims. Given that the method step of the '008 patent and the instant claims is the same, and the amylin agonist administered and the amount administered are the same as the ones described in the instant specification, the method of the '008 patent is expected to bring about a obesity-treating effect, weight gain-inhibiting effect, or weight loss-inducing effect in Beumont's intrinsically obese calcitonin-treated diabetic patient as defined in the instant invention. Since the structural limitations of the instantly claimed method and all of the criteria required by the instant claims are met by the teachings of the '008 patent, Beumont's ('008) method is expected to serve necessarily as the instantly claimed method and is expected to bring about the obesity-treating effect, weight gain

inhibiting effect, or weight loss-inducing effect. The Office's position that Beumont's ('008) method is the same as the Applicants' claimed method is based upon the fact that the method step, the amylin agonist calcitonin administered and its amount administered, the subcutaneous route by which the amylin agonist is administered, and the at least one intrinsically obese diabetic human patient to which the amylin agonist is administered, are the *same* in the two methods. The art-recognized intrinsic obesity being prevalent in 80 to 90% of diabetic patients as disclosed by Tsanev (see abstract), Beumont's ('008) method of administration of the above-identified therapeutically effective amount (i.e., dosage units of about 0.1 to 1 mg) of the amylin agonist calcitonin to at least one intrinsically obese type 2 diabetic human subject anticipates the instant claims. Given that the method step of the Beumont's ('008) method and the instant claims are the same, Beumont's ('008) method is expected to bring about the weight gain-inhibiting, weight loss-causing or obesity-treating effect in the intrinsically obese calcitonin-treated insulin-requiring human diabetic patient of Beumont's ('008) patent. Since the Office does not have the facilities for examining and comparing Applicants' claimed method with that of the prior art, the burden is on Applicants to show a novel difference between the claimed method and the method of the prior art. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald et al.*, 205 USPQ 594. MPEP 2112 refers to *In re Best* to explain that something which is old does not become patentable upon the discovery of a new property; 'the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. *In re Best*, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977)'. Since the prior art clearly teaches the instantly claimed method, any assertions of specific functional properties attributed to the amylin agonist calcitonin in the claimed method are merely inherent and do not necessarily make the claimed method patentable.

Claims 7, 14 and 16 are clearly anticipated by Beumont *et al.* ('008). The publication of Tsanev is **not** used as a secondary reference in combination with the reference of Beumont *et al.* ('008), but rather is used to show that every element of the claimed subject matter is disclosed by Beumont *et al.* ('008) with the unrecited limitation(s) being inherent as evidenced by the state of the art. See *In re Samour* 197 USPQ 1 (CCPA 1978). 'To serve as an anticipation when the reference is silent about the asserted inherent characteristic, such gap in the reference may be filled with recourse

to extrinsic evidence. Such evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill.' *Continental Can Co. USA v. Monsanto Co.*, 948 F.2d 1264, 1268, 20 USPQ2d 1746, 1749 (Fed. Cir. 1991). Note that as long as there is evidence of record establishing inherency, failure of those skilled in the art to contemporaneously recognize an inherent property, function or ingredient of a prior art reference does not preclude a finding of anticipation. *Atlas Powder Co. v. IRECO Inc.*, 190 F.3d 1342, 1349, 51 USPQ2d 1943, 1948 (Fed. Cir. 1999). See MPEP 2124. Tsanev's extrinsic evidence makes clear that the missing descriptive matter, i.e., prevalence of obesity in at least one of Beumont's insulin-requiring diabetic subjects administered with calcitonin, is necessarily present in the thing described by Beumont *et al.* ('008). The method of Beumont *et al.* ('008) clearly anticipates the claimed method of the instant invention, because Beumont *et al.* ('008) taught the very step of the instantly claimed method in the very same diabetic human patient. The alleged failure of Beumont *et al.* ('008) to expressly mention treatment of obesity as a goal is irrelevant. To the extent the method embodiment in the claimed invention achieves treatment of obesity, so does the method of Beumont *et al.* ('008). Where the result is a necessary consequence of what was deliberately intended, it is of no import that the article's authors did not appreciate the results. See *Mehl/Biophile International Corp. v. Milgraum*, U.S. Court of Appeals Federal Court, 52 USPQ2d 1303 and 1306, 192 F3d 1362, 1999 citing *W.L. Gore & Assocs. v. Garlack, Inc.*, 721 F.2d 1540, 1548, 220 USPQ 303, 309 (Fed. Cir. 1983).

35) Claims 7, 14, 16 and 17 are rejected under 35 U.S.C § 102(e)(2) as being anticipated by Gaeta *et al.* (US 5,686,411, already of record) ('411) as evidenced by Tsanev (*Vutr. Boles* 23: 12-17, 1984, abstract, already of record).

The limitation 'consisting essentially of' in claim 16 and the limitation 'method ... comprising ..... wherein said compound is not administered in conjunction with another obesity relief agent' in claim 14 do not exclude the presence of an anti-diabetic agent, insulin, glucagon, a gastric emptying-inhibiting agent etc. in the recited composition.

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 C.F.R 1.132 that

any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention 'by another', or by an appropriate showing under 37 C.F.R 1.131.

Gaeta *et al.* ('411) taught a method of administering to a mammal having diabetes mellitus, including a patient seen by a medical practitioner, i.e., a human, a therapeutically effective amount of the amylin agonist of claim 19, ^{25,28,29}Pro-human amylin (SEQ ID NO: 1 or pramlintide). See claims 34, 35 and 19; and lines 45-53 in column 7 of the '411. Gaeta *et al.* ('411) taught the 'therapeutically effective amount' of the amylin agonist to include the dosage units of 0.1 to 5 mg or 0.5 to 1.0 mg of the amylin agonist. See lines 53-59 in column 8. The amount effective to treat obesity, inhibit weight gain, or induce weight loss encompassed in the instant claims as described in the instant application, for example, about 0.01 milligrams to about 5 milligrams per day, about 0.05 milligrams to about 2 milligrams per day, or 300 micrograms per dose, falls within the range of therapeutically effective amount of the amylin agonist disclosed in the '411 patent. Lines 9-14 of column 3 of the U.S. patent '411 describe that the limitation 'diabetes mellitus' includes insulin-requiring diabetes mellitus and that the administration is of amylin agonist analogue *alone*. The amylin agonist composition comprises a pharmaceutical carrier and the amylin agonist without insulin or glucagon. See lines 9-11 in column 7 and lines 37-39 in column 8. Given the art-known prevalence of intrinsic obesity in 80% to 90% of diabetic patients as disclosed by Tsanev (see abstract), at least one of the diabetic patients administered with the amylin agonist ^{25,28,29}Pro-human amylin in the method disclosed by the '411 patent qualifies as a human patient in need of treatment for obesity. Therefore, the method of the '411 patent comprising the administration of 0.1 to 5 mg, or 0.5 to 1.0 mg of the amylin agonist ^{25,28,29}Pro-human amylin to a diabetic human anticipates the instant claims. Given that the method step of the '411 patent and the instant claims are the same, the amylin agonist, ^{25,28,29}Pro-human amylin, administered and the amount administered are the same, the method of the '411 patent is expected to bring about a therapeutic effect, weight gain-inhibiting effect, and weight loss-inducing effect in the intrinsically obese ^{25,28,29}Pro-human amylin-treated insulin-requiring diabetic patient of Gaeta ('411) as defined in the instant invention. Since the structural limitations of the instantly claimed method and all of the criteria required by the instant claims are met by the teachings of the '411 patent, Gaeta's ('411) method is expected to

serve necessarily as the instantly claimed method and is expected to bring about the obesity-treating effect, weight gain-inhibiting effect, or weight loss-inducing effect. The Office's position that Gaeta's ('411) method is the same as the Applicants' claimed method is based upon the fact that the method step, the amylin agonist, ^{25,28,29}Pro-human amylin administered, the amount of the ^{25,28,29}Pro-human amylin administered, and the at least one intrinsically obese diabetic human patient to whom the ^{25,28,29}Pro-human amylin is administered, are the *same* in the two methods. The art-recognized intrinsic obesity being prevalent in 80 to 90% of diabetic patients as disclosed by Tsanev (see abstract), Gaeta's ('411) method of administration of the above-identified therapeutically effective amount (i.e., 0.1 to 5 mg, or 0.5 to 1.0 mg) of the amylin agonist ^{25,28,29}Pro-human amylin to at least one intrinsically obese type 2 diabetic human subject anticipates the instant claims. Given that the method step of the Gaeta's ('411) method and the instant claims are the same, Gaeta's ('411) method is expected to bring about the weight gain-inhibiting, weight loss-causing, or obesity-treating effect against the intrinsic obesity in the ^{25,28,29}Pro-human amylin-treated, insulin-requiring human diabetic patient. Since the Office does not have the facilities for examining and comparing Applicants' claimed method with that of the prior art, the burden is on Applicants to show a novel difference between the claimed method and the method of the prior art. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald et al.*, 205 USPQ 594. MPEP 2112 refers to *In re Best* to explain that something which is old does not become patentable upon the discovery of a new property; 'the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. *In re Best*, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977)'. Since the prior art clearly teaches the instantly claimed method, any assertions of specific functional properties attributed to the amylin agonist ^{25,28,29}Pro-human amylin in the claimed method are merely inherent and do not necessarily make the claimed method patentable.

Claims 7, 14 and 16 are clearly anticipated by Gaeta *et al.* ('411). The publication of Tsanev is **not** used as a secondary reference in combination with the reference of Gaeta *et al.* ('411), but rather is used to show that every element of the claimed subject matter is disclosed by Gaeta *et al.* ('411) with the unrecited limitation(s) being inherent as evidenced by the state of the art. See *In re Samour* 197 USPQ 1 (CCPA 1978). 'To serve as an anticipation when the reference is silent about

the asserted inherent characteristic, such gap in the reference may be filled with recourse to extrinsic evidence. Such evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill.' *Continental Can Co. USA v. Monsanto Co.*, 948 F.2d 1264, 1268, 20 USPQ2d 1746, 1749 (Fed. Cir. 1991). Note that as long as there is evidence of record establishing inherency, failure of those skilled in the art to contemporaneously recognize an inherent property, function or ingredient of a prior art reference does not preclude a finding of anticipation. *Atlas Powder Co. v. IRECO Inc.*, 190 F.3d 1342, 1349, 51 USPQ2d 1943, 1948 (Fed. Cir. 1999). See MPEP 2124. Tsanev's extrinsic evidence makes clear that the missing descriptive matter, i.e., prevalence of obesity in at least one of Gaeta's ('411) insulin-requiring diabetic subjects administered with ^{25,28,29}Pro-human amylin, is necessarily present in the thing described by Gaeta *et al.* ('411). The method of Gaeta *et al.* ('411) clearly anticipates the claimed method of the instant invention, because Gaeta *et al.* ('411) taught the very step of the instantly claimed method in the very same diabetic human patient. The alleged failure of Gaeta *et al.* ('411) to expressly mention treatment of obesity as a goal is irrelevant. To the extent the method embodiment in the claimed invention achieves treatment of obesity, so does the method of Gaeta *et al.* ('411). Where the result is a necessary consequence of what was deliberately intended, it is of no import that the article's authors did not appreciate the results. See *Mehl/Biophile International Corp. v. Milgraum*, U.S. Court of Appeals Federal Court, 52 USPQ2d 1303 and 1306, 192 F3d 1362, 1999 citing *W.L. Gore & Assocs. v. Garlack, Inc.*, 721 F.2d 1540, 1548, 220 USPQ 303, 309 (Fed. Cir. 1983).

36) Claims 1-7, 9, 11-14, 16 and 17 are rejected under 35 U.S.C § 102(b) as being anticipated by Kolterman *et al.* (*Diabetologia* 39: 492-499, April, 1996, already of record) (Kolterman *et al.*, 1996) as evidenced by Itasaka *et al.* (*Psychiatr. Clin. Neurosci.* 54: 340-341, June 2000, already of record).

It is noted that the human patient in need of the recited treatment according to the instant invention is expressly identified in the instant specification as one having a body weight of 79 kg. A 70 kg patient is not excluded from the scope of the instant invention 'as a human subject in need thereof', but is expressly included. The recited therapeutic amount range of 'about 0.1 milligrams per day to about 1 milligram per day', or 'about 0.01 to about 5 mg/day', or 0.03 to

about 5 mg/day of the amylin agonist or amylin agonist analogue, pramlintide, administered is specifically "for a 70 kg patient". See lines 4-8 of page 23 of the substitute specification; and paragraph bridging pages 23 and 24 and lines 3-7 on page 24 of Applicants' response filed December 2002.

Kolterman *et al.* (1996) taught a method of subcutaneous administration of 30, 100, or 300 μg of pramlintide composition or AC137 (i.e., $^{25, 28, 29}$pro-h-amylin or SEQ ID NO: 1), a human amylin analogue, to human patients with insulin-dependent diabetes mellitus or IDDM who are on insulin. Pramlintide is administered three times daily for a period of 14 days. See abstract; and page 493. The mean body weight ± SEM of diabetic patients included in Kolterman's (1996) method who were administered subcutaneously with 30 micrograms, 100 micrograms, and 300 micrograms of pramlintide, three times a day for 14 days, was 70.6 ± 2.7, 74.4 ± 2.5, and 75.7 ± 2.6 respectively. Therefore, the 70.6 to 75.7 kg insulin-taking diabetic patients from Kolterman's (1996) study qualify as human subjects in need of treatment for obesity as recited in the instant claims. Additionally, even BMI-wise, Kolterman's (1996) diabetic subjects meet the limitation 'a human subject .... in need of treatment for obesity' as recited in the instant claims, because the diabetic subjects included in Kolterman's method (1996) had a BMI of up to 27. See second full paragraph under 'Subjects, materials and methods. Therefore, Kolterman's (1996) diabetic subjects having a BMI at least in the range of 24 up to 27 do qualify as diabetic subjects in need of treatment for obesity in light of what is known in the art. For example, Itasaka *et al.* teach that a BMI of 24.0 to 26.4 represents mild obesity and 26.4 and heavier (i.e., including a BMI of 26.4 to 27) represents obesity in humans (see abstract of Itasaka *et al.*). Kolterman's (1996) pramlintide composition did not comprise another obesity relief agent, but consisted of or consisted essentially of pramlintide. The pramlintide composition was injected subcutaneously to the human patients (see 'Study design') and therefore is expected to inherently contain a pharmaceutically acceptable carrier therein. The amount administered was 30 micrograms three times a day to 'about 0.1 milligrams' or 300 micrograms per day. See 'Study design'; Table 1; and paragraph there below. Kolterman's (1996) subcutaneous administration of a therapeutically effective amount of the amylin agonist ^{25,28,29}Pro-human amylin to diabetic human subjects on insulin weighing 70 kg or more, or having a BMI falling in the BMI range of 24 up to 27, anticipates the instant claims. Thus, the very active

step recited in the instantly claimed method was disclosed and practiced by Kolterman *et al.* in April, 1996. Given that the method step in Kolterman's (1996) method and the instant claims are the *same*, and the amylin agonist analogue pramlintide administered and its amount administered are the *same*, Kolterman's (1996) method is expected to necessarily bring about the same weight gain-inhibiting (i.e., maintaining of existing body weight) or weight loss-inducing therapeutic effect in Kolterman's (1996) pramlintide-treated diabetic patients who are on insulin. Since the Office does not have the facilities for examining and comparing Applicants' claimed method with that of the prior art, the burden is on Applicants to show a novel difference between the claimed product and the product of the prior art. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald et al.*, 205 USPQ 594. MPEP 2112 refers to *In re Best* to explain that something which is old does not become patentable upon the discovery of a new property; 'the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. *In re Best*, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977)'. Since the prior art clearly teaches the claimed method, any assertions of specific functional properties attributed to the amylin agonist pramlintide in the claimed method are merely inherent and do not necessarily make the claimed method patentable. The prior art method of administering the above-explained amount of the amylin agonist ^{25,28,29}Pro-human amylin (pramlintide or SEQ ID NO: 1) to insulin-taking diabetic human subjects weighing 70 kg or more, and/or having a BMI falling in the range of 24 up to 27 necessarily serves as the Applicants' method of treating obesity by inhibiting weight gain or inducing weight loss, as claimed currently.

Claims 1-7, 9, 11-14, 16 and 17 are anticipated by Kolterman *et al.* (1996). The publication of Itasaka *et al.* is **not** used as a secondary reference in combination with the reference of Kolterman *et al.* (1996), but rather is used to show that every element of the claimed subject matter is disclosed by Kolterman *et al.* (1996) with the unrecited limitation(s) being inherent as evidenced by the state of the art. See *In re Samour* 197 USPQ 1 (CCPA 1978). 'To serve as an anticipation when the reference is silent about the asserted inherent characteristic, such gap in the reference may be filled with recourse to extrinsic evidence. Such evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill.' *Continental Can Co. USA v.*

Monsanto Co., 948 F.2d 1264, 1268, 20 USPQ2d 1746, 1749 (Fed. Cir. 1991). Note that as long as there is evidence of record establishing inherency, failure of those skilled in the art to contemporaneously recognize an inherent property, function or ingredient of a prior art reference does not preclude a finding of anticipation. *Atlas Powder Co. v. IRECO Inc.*, 190 F.3d 1342, 1349, 51 USPQ2d 1943, 1948 (Fed. Cir. 1999). See MPEP 2124. Itasaka's extrinsic evidence makes clear that the missing descriptive matter, i.e., prevalence of obesity in at least one of Kolterman *et al.* (1996) insulin-taking diabetic subjects administered with ^{25,28,29}Pro-human amylin, is necessarily present in the thing described by Kolterman *et al.* (1996). The method of Kolterman *et al.* (1996) clearly anticipates the claimed method of the instant invention, because Kolterman *et al.* (1996) taught the very step of the instantly claimed method in the diabetic human patient. The alleged failure of Kolterman *et al.* (1996) to expressly mention treatment of obesity as a goal is irrelevant. To the extent the method embodiment in the claimed invention achieves treatment of obesity, so does the method of Kolterman *et al.* (1996). Where the result is a necessary consequence of what was deliberately intended, it is of no import that the article's authors did not appreciate the results. See *Mehl/Biophile International Corp. v. Milgraum*, U.S. Court of Appeals Federal Court, 52 USPQ2d 1303 and 1306, 192 F3d 1362, 1999 citing *W.L. Gore & Assocs. v. Garlack, Inc.*, 721 F.2d 1540, 1548, 220 USPQ 303, 309 (Fed. Cir. 1983).

Remarks

37) Claims 1-7 and 9-17 stand rejected.

38) Applicants' amendments necessitated the new ground(s) of rejection presented in this Office action. **THIS ACTION IS MADE FINAL.** Applicants are reminded of the extension of time policy as set forth in 37 C.F.R 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

39) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. The Fax number for submission of amendments, responses and/or papers is (571) 273-8300, which receives transmissions 24 hours a day and 7 days a week.

40) Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAG or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.Mov. Should you have questions on access to the Private PAA system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (in USA or CANADA) or 571-272-1000.

41) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (571) 272-0854. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 7.15 a.m. to 4.15 p.m. except one day each bi-week, which would be disclosed on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's Supervisor, Shanon Foley, can be reached on (571) 272-0898.

January, 2008

S. DEVI, PH.D.
PRIMARY EXAMINER